



FEMALE GENITAL SYSTEM PATHOLOGY

Lec. 3

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Case scenario

A 28-year-old woman attends the colposcopy clinic after an abnormal cytology pap smear test. She complains of postcoital bleeding.

She was diagnosed with genital herpes virus several years ago.

Examination

The cervix is macroscopically normal.

At colposcopy, acetic acid is applied and an irregular white area is apparent to the left of the os. Lugol's iodine is applied and the same area stains pale while the rest of the cervix stains dark brown. A biopsy is taken.

Objectives of this lecture

At the end of the lecture

- Anatomy and normal histology of cervix (rapid revision)
- Classification of cervical pathological disorders
- Intraepithelial neoplasia
- Invasive disease (cervical cancer)
- ❖ Types
- ❖ Presentation
- ❖ Histopathological finding

The cervix disorders:

Anatomy :-

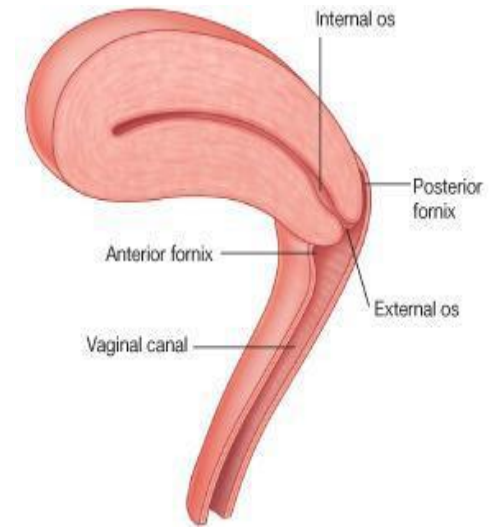
Cervix is The elongated lower part of the uterus that communicates above with the uterine cavity at the internal Os and below with the vagina at the external Os.

Measuring 2.5-3.0 cm.

Divided by the vaginal attachment into

- supravaginal portion above
- vaginal portion (portio-vaginalis) below.

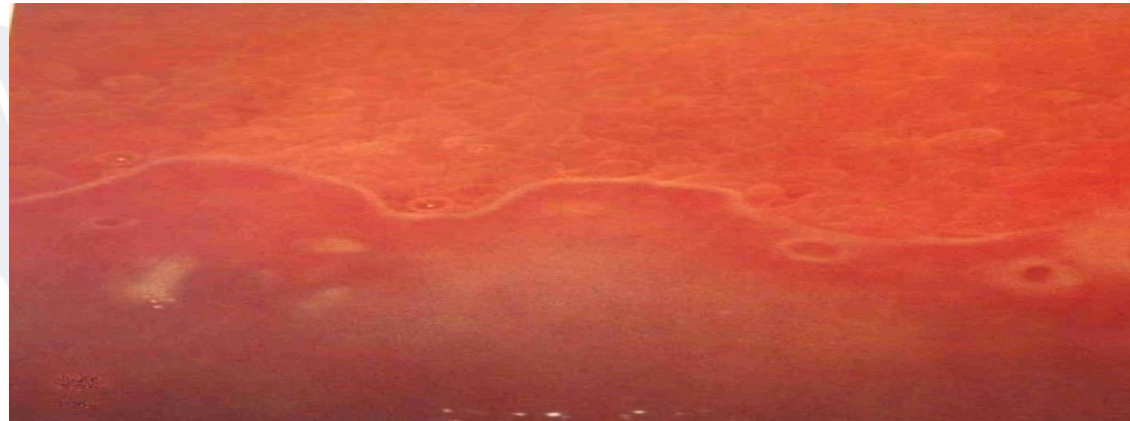
- **Endocervix:** Lined by simple columnar epithelium with compound glands or crypts that are liable to chronic infection. It secretes alkaline cervical mucus.
- **Muscle layer:** Outer longitudinal and inner circular muscles.(2 layers only)
- **Ectocervix:** Formed of stratified squamous epithelium covering the outer portion of the cervix. The junction between squamous and columnar epithelium at the external os is either abrupt or it may form a transitional zone 1-3 mm known as the transformation zone.



Squamocolumnar Junction

Squamous metaplasia :-

is the change of the endocervical columnar epithelial to squamous epithelial due to high vaginal acidity . It is a premalignant lesion may be seen in the context of benign lesions (e.g., atypical polypoid adenomyoma), chronic irritation, or cancer (e.g., endometrioid endometrial carcinoma), as well as pleomorphic adenoma.



Close-up of SCJ

Premalignant and Malignant Cervical Neoplasms

CERVICAL INTRAEPITHELIAL NEOPLASIA

Pathogenesis

- Risk factors
 - HPV
 - Early marriage
 - Multiple sexual pattern
 - Male pattern & deviation
 - Smoking
 - Immune deficiency
- High oncogenic risk HPV types:
 - HPV 16 (60% of cervical cancer)**
 - HPV 18 (10% of cervical cancer).**
- Most HPV infections are asymptomatic and do not cause any tissue changes
- 50% are cleared within 8 months & in 90% cleared within 2 years.
- Persistent infection (as with high-risk types or immunocompromise) increases the risk of developing malignancy.

Cervical Intraepithelial Neoplasia

Precancerous cervical epithelial histologic changes

Classified as :-

Low - grade or High - grade squamous intraepithelial lesions (LSIL and HSIL, respectively).

More than 80% of LSIL and 100% of HSIL lesions are associated with high-risk HPV;

HPV 16 is the most common type associated with both.

- **In LSIL, the atypia is confined to the basal third of the epithelium.**

- 60% of LSIL spontaneously regress within 2 years,
- 30% persist over that period;
- only 10% progress to HSIL,
- LSIL does not proceed directly to invasive carcinoma.
- It is therefore not treated like a premalignant lesion.

HSIL exhibit moderate to severe dysplasia and **extends to two thirds (or more) of the epithelial thickness.**

- **Also includes carcinoma in situ.**
- 30% of HSIL will regress over 2 years,
- 60% will persist,
- 10% will progress to carcinoma within a 2- to 10-year period.

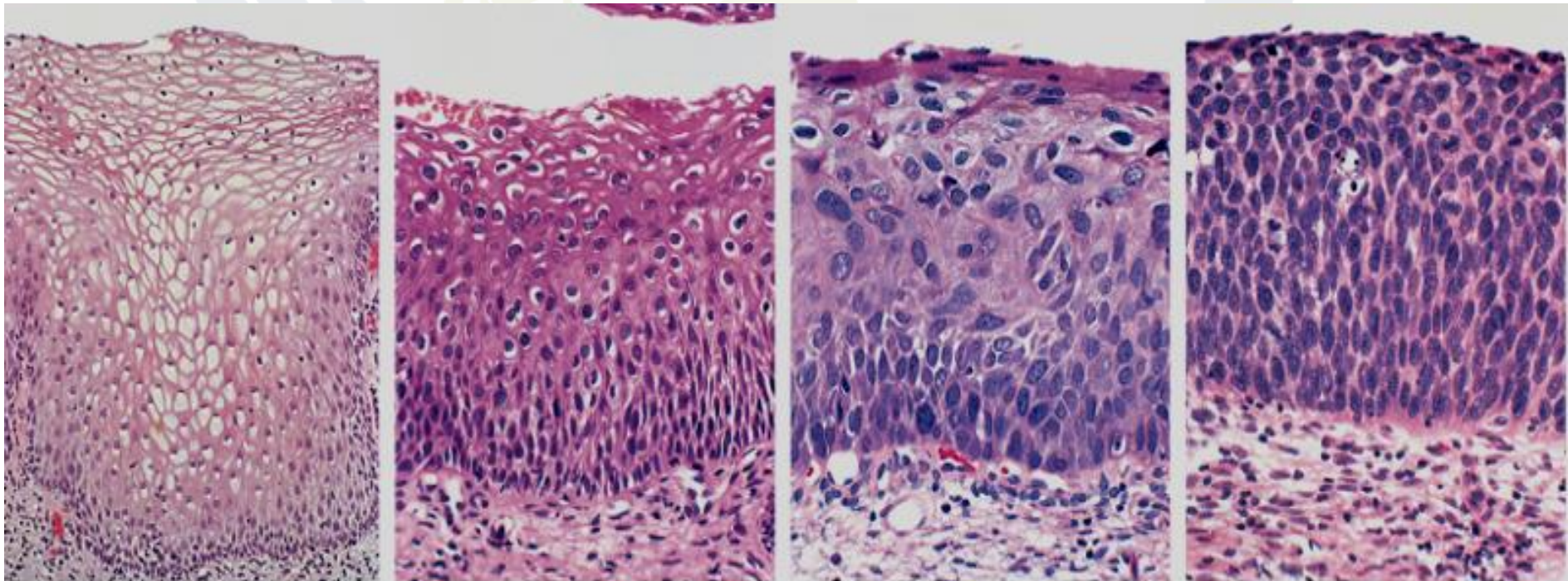
CIN

- **Grades:**

*CIN-I (mild dysplasia) - mild changes - only in the lower 1/3

*CIN-II (moderate dysplasia) - moderate change - in the lower 2/3

*CIN-III (severe dysplasia-CIS) - severe changes - full thickness



Normal

CIN I

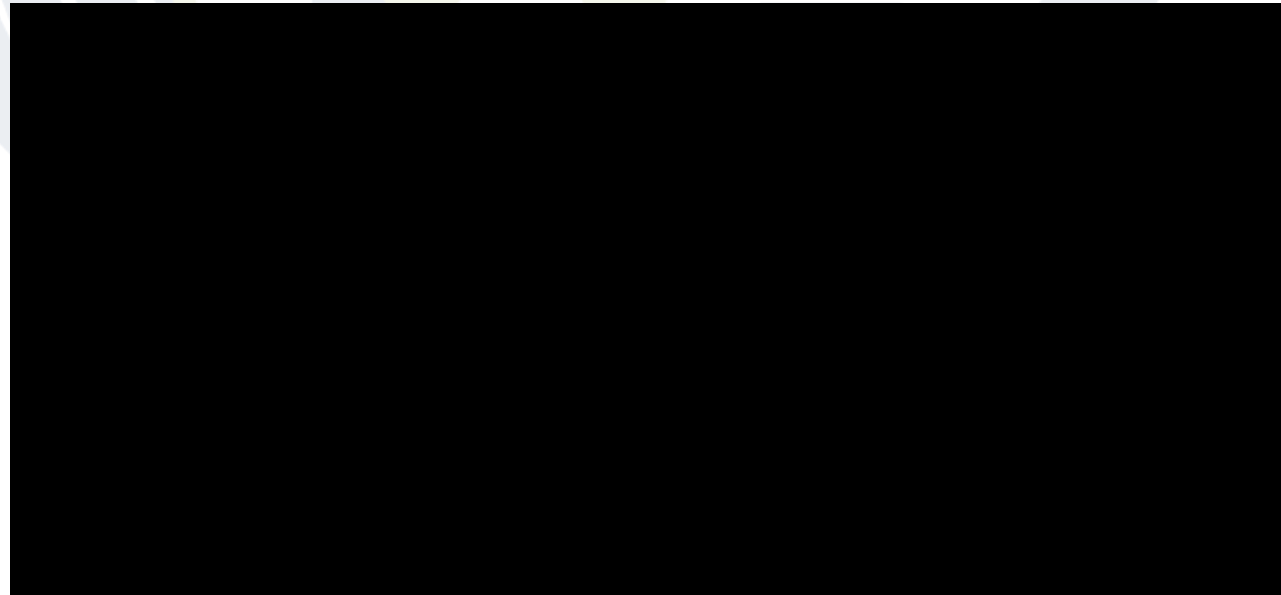
CIN II

CIN III

Clinically :- often asymptomatic but occasionally with contact bleeding

Diagnosis :

- **Pap smear cytology :- Papanicolaou test** is a method of cervical screening used to detect potentially precancerous and cancerous processes in the cervix or colon (in both men and women).
- Abnormal findings are often followed up by more sensitive diagnostic procedures or interventions to prevent progression to cervical cancer.
- A procedure in which a small brush or spatula is used to gently remove cells from the cervix so they can be checked under a microscope for cervical cancer or cell changes that may lead to cervical cancer.



Colposcopic examination & biopsy.

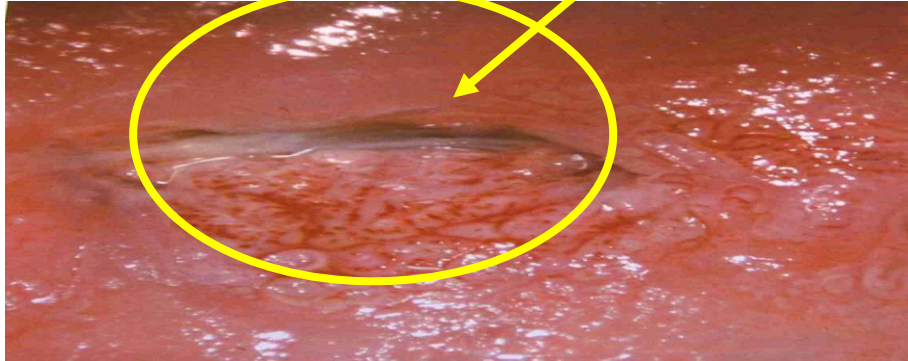
is a medical diagnostic procedure to visually examine the cervix as well as the vagina and vulva using a colposcope which provides a magnified and illuminated view of the areas, allowing the colposcopist to visually distinguish normal from abnormal appearing tissue, such as damaged or abnormal changes in the tissue , and take directed biopsies for further pathological examination if needed



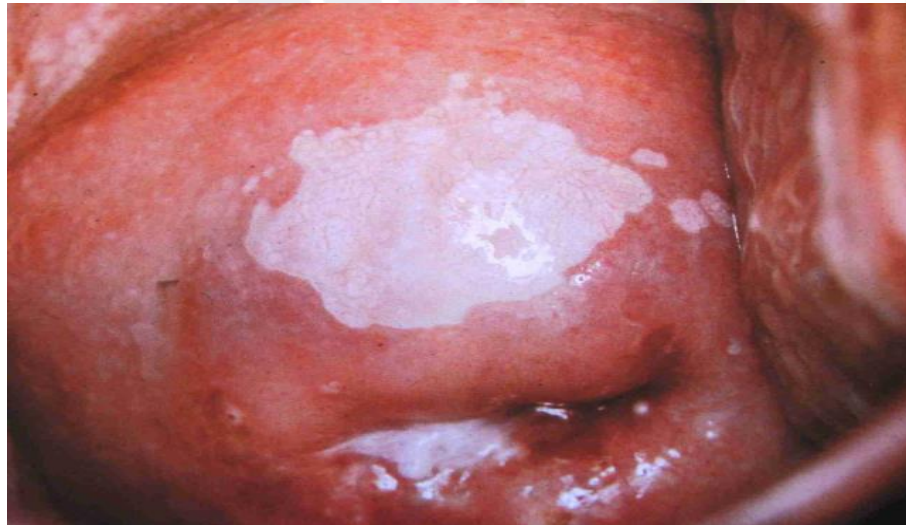
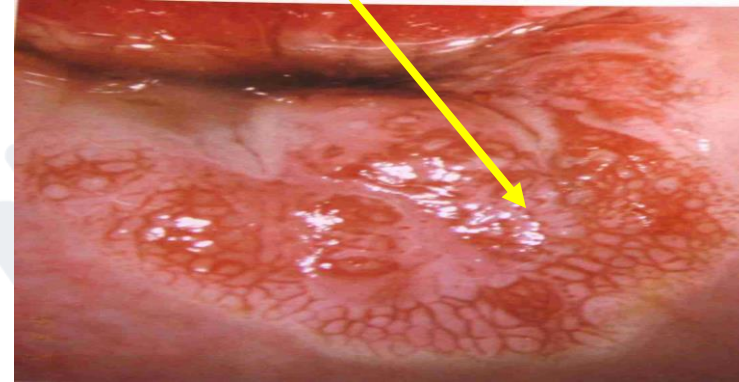
Colposcopy

Gross:

Punctations



Mosaicism



Post Acetic Acid



Acetowhite changes

Cervical cancer

- **Worldwide, cervical cancer is both the 4th -most common cause of cancer and deaths from cancer in women**
- **It is the 2^{ed} -most common cause of female-specific cancer after breast cancer, accounting for around 8% of both total cancer cases and total cancer deaths in women.**
- **About 80% of cervical cancers occur in developing countries.**
- **It is the most frequently detected cancer during pregnancy, with an occurrence of 1.5 to 12 for every 100,000 pregnancies.**
- **80% % is squamous cell carcinoma**
- **15% adenocarcinoma**
- **Adenosquamous and neuroendocrine carcinomas collectively amount to 5%.**
- **All are associated with high-risk HPV**
- **Peak age incidence :- 45 years old or 2-10 years after discover of HSIL**

Risk factors [the same of CIN]

- ❖ **Human papillomavirus**
- ❖ **Smoking** :- Cigarette smoking, both active and passive, increases the risk of cervical cancer.
- ❖ **Oral contraceptives pills** :- (Long-term use) 5 to 9 years have about **three** times the incidence of invasive cancer, and those who used them for 10 years or longer have about **four** times the risk
- ❖ **Multiple pregnancies** :- **seven or more full-term pregnancies have around four times the risk of cancer compared with women with no pregnancies, and two to three times the risk of women who have had one or two full-term pregnancies.**
- ❖ **Multiple sexual partners**
- ❖ **A male partner with multiple previous or current sexual partners**
- ❖ **Young age at first intercourse**
- ❖ **Immunosuppression**

Diagnosis

- Increasingly , cervical cancers are detected at **subclinical** stages by **routine Pap smear screening**.

Clinically :-

- ❖ The early stages of cervical cancer may be completely **free of symptoms**.
- ❖ Or it can be cause
 - Vaginal bleeding (one most common form being bleeding after sexual intercourse), bleeding after vaginal douching or after a pelvic exam
 - Moderate pain during sexual intercourse or during urination
 - Vaginal discharge leucorrhea
 - or (rarely) a vaginal mass.
 - **Symptoms of advanced cervical cancer may include**: loss of appetite, weight loss, fatigue, pelvic pain, back pain, leg pain, swollen legs, heavy vaginal bleeding, bone fractures, and (rarely) leakage of urine or feces from the vagina.

Investigation :-

General Ix

Imaging study

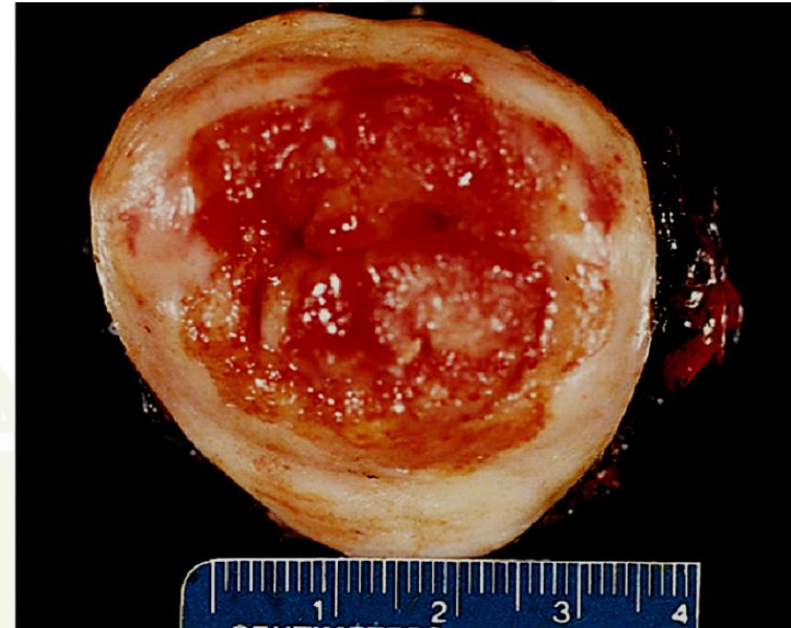
Histopathology

Morphology

Grossly: Lesions can be exophytic or infiltrative.

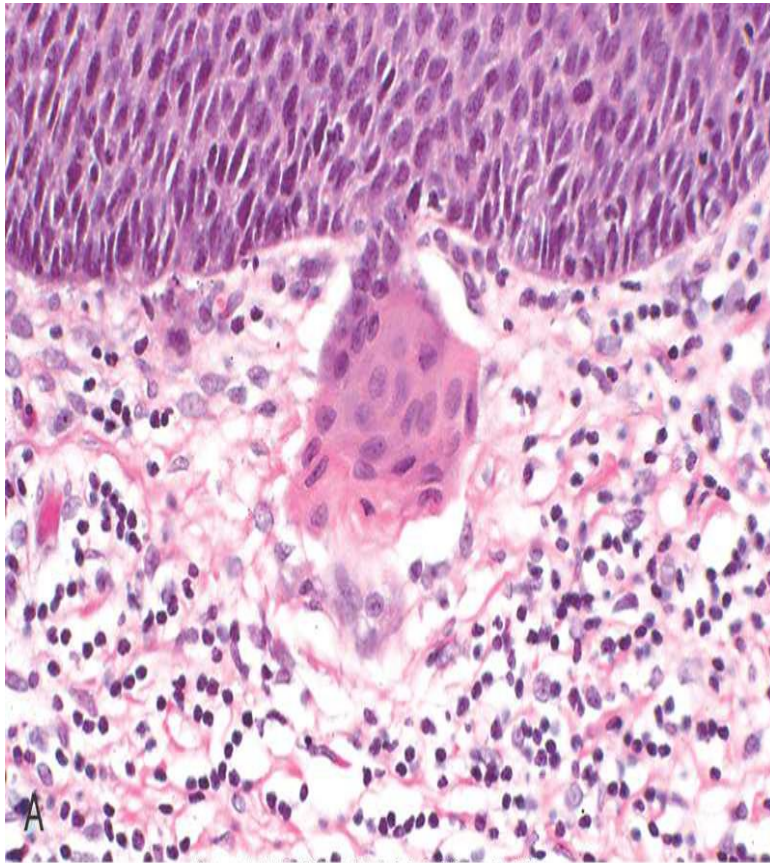


This is the gross appearance of a cervical squamous cell carcinoma that is **still limited to the cervix** (stage I). The tumor is a **fungating red to tan to yellow mass**.



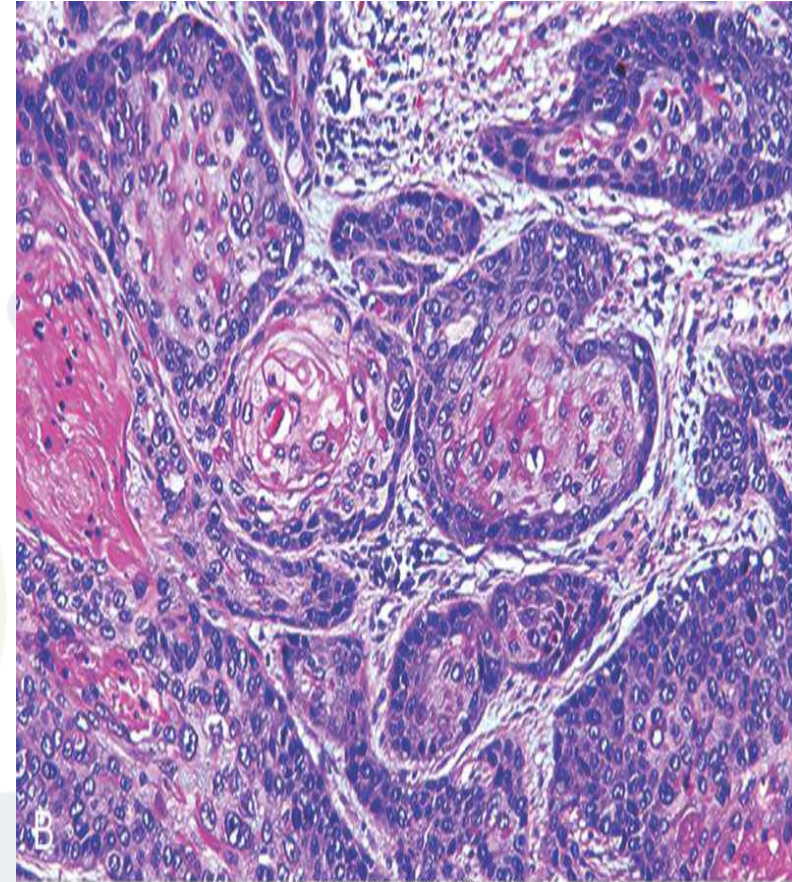
Pink-tan, Friable , Fungating (exophytic) lesion on the anterior cervical lip

Microscopically



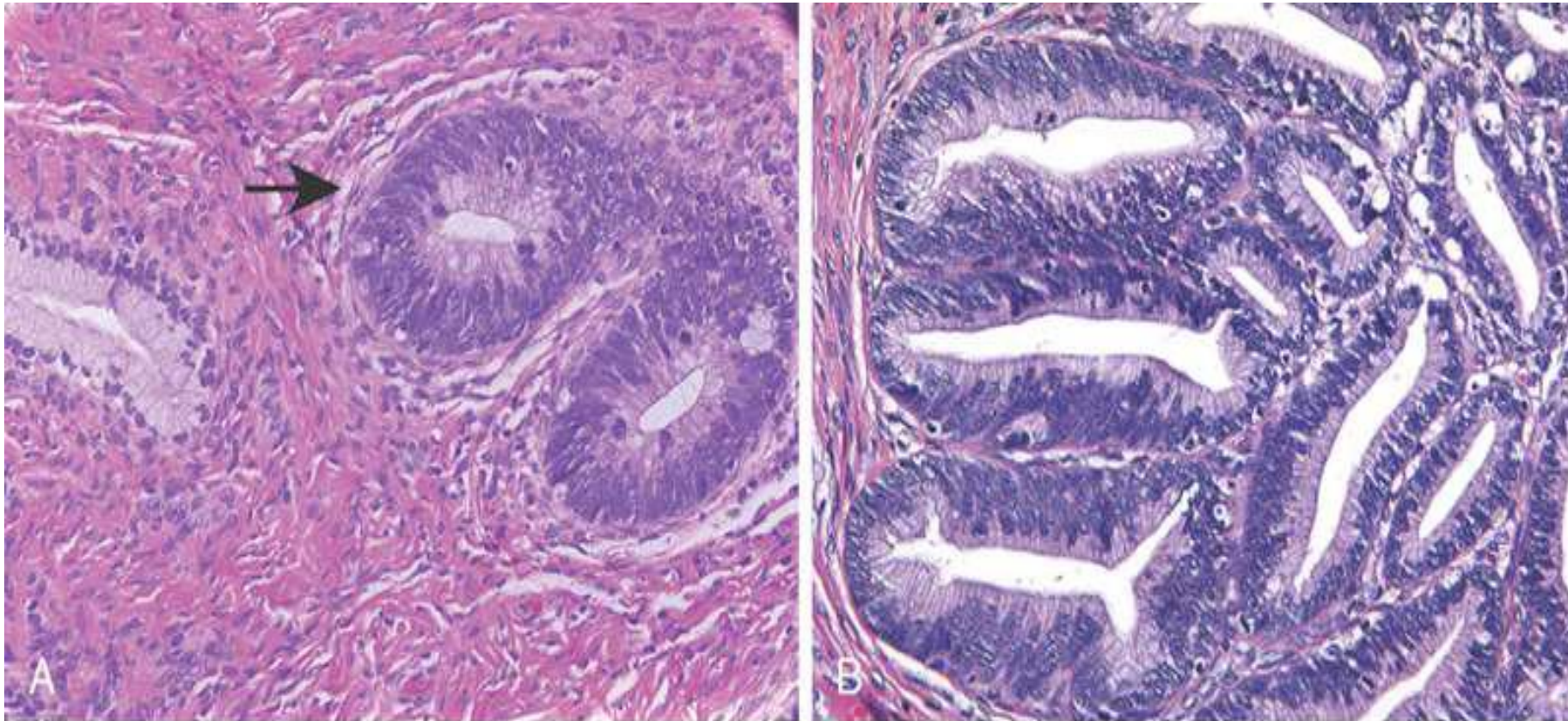
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Squamous cell carcinoma of the cervix
Microinvasive squamous cell carcinoma with *invasive nest* breaking through the basement membrane of HSIL



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squamous cell carcinomas are composed of nests and tongues of malignant squamous epithelium either keratinizing or non keratinizing invading the underlying cervical stroma



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Adenocarcinomas are characterized by proliferation of glandular epithelium composed of malignant endocervical cells with large, hyperchromatic nuclei and relatively mucin-depleted cytoplasm, resulting in dark appearance of the glands as compared with the normal endocervical epithelium

- **Spread**

- **Locally** :- to vagina ; uterus ; bladder ; rectum
- **Lymphatic** :- early to iliac ; aortic ; pelvic ; inguinal LN
- **Bloody** :- late to distant places

Staging by the International Federation of Gynecology and Obstetrics (FIGO) staging system, which is based on clinical examination, rather than surgical findings : inspection, palpation, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography, and X-ray examination of the lungs and skeleton, & **Depend on clinical spread**

- Stage zero :- pre invasive ca
- Stage I :- confined to cervix
- Stage II :- beyond cervix but not to pelvis
- Stage III:- ca cx & \or lower third of vagina & \or non function kidney
- Stage IV:- invade bladder & rectum & \or beyond pelvis & \or distant metastasis

Prognosis

- Stage zero :- 100%
- Stage I :- 90%
- Stage II :- 82%
- Stage III :- 35%
- Stage IV :- 10%

Prevention :-

- **Screening**
- **Barrier protection:-** Barrier protection and/or spermicidal gel use during sexual intercourse decreases cancer risk
- **HPV Vaccination**
- **Nutrition :-** Vitamin A is associated with a lower risk as are vitamin B12, vitamin C, vitamin E, and beta-Carotene

THANK YOU
FOR YOUR
ATTENTION